

CARDIOVASCULAR

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A., INC. HISTORY

COMMITTEE

Dr. Bing
Dr. Cattell
Dr. Jacobson

110 EAST 59TH STREET
NEW YORK, N. Y. 10022

No. 519BR-1

519B

519A 5/1/69-6/1/72

519 2/1/66-2/1/69

CF 374 2/1/63-2/1/66

Application For Renewal of Research Grant

First ☒

Second ☐

Date:

January 16, 1973

1. Name of Investigator(s): (include title and degrees)

Louis A. Soloff, M.D.
Professor of Medicine

2. Institution &

Address:

Temple University Health Sciences Center
3400 North Broad Street
Philadelphia, Penna. 19140

3. Short Title of Project:

Purification and physiologic significance of lecithin cholesterol acyl transferase (LCAT).

4. Proposed Renewal Starting Date: (Anniversary or other)

June 1, 1973

5. Discuss any Important Changes or Additions to Objectives or Specific Aims:

Our objective and specific aims have not changed: to increase fundamental information concerning the metabolism of blood cholesterol, which occupies the center of the predominant theory of the pathogenesis of atherosclerosis. Our approaches are 1) to purify lecithin:cholesterol acyl transferase (LCAT), the enzyme responsible for esterification of plasma cholesterol. In the past, the major obstacle to solution of this problem has been instability of the enzyme (half life 3.5 hours) once a certain stage of purification has been achieved. This year we have been able to obtain a preparation which is highly purified and appears stable for weeks or possibly months, a feat, to my knowledge not yet accomplished elsewhere. The preparation is approximately 1500 fold concentrated if LCAT activity divided by the absorption at 280 nm is used as the index of purification. This preparation is obtained after affinity chromatography, and contains one major and about three minor components as judged by disc gel electrophoresis. Preliminary experiments indicate that LCAT activity is associated with the major component. 2) At the same time, we are determining the physiologically important initial rate of esterification of plasma cholesterol in a variety of disorders and changes in this rate produced by physiologic, pharmacologic and hormonal stimuli and also by smoking. Publications listed under (10) represent the types of work we have done in 1972. In addition, manuscripts will soon be prepared on (a) LCAT activity during the menstrual cycle. (b) LCAT activity in the fasting and fed rat (c) interactions between post heparin lipolytic activity and LCAT (d) a hypothesis explaining competitive inhibition of free fatty acids and lysolecithin (a product of LCAT) on LCAT activity (e) arterial wall, RBC and plasma contributions to LCAT activity.

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6. Give a Brief Statement of your Working Hypothesis if altered or modified:

JAN 23 1973

7. Changes or Additions to Experimental Design and Procedures: (Attach Separate Pages)

None

8. Additional Requirements:

Gas chromatograph:

At the present time we are using the gas chromatograph in the Clinical Research Center. This apparatus is also being used by four other active research workers so that it is available to us only part-time. Furthermore the Clinical Research Center is on the second floor of the hospital and our laboratory is on the fifth floor of the chemical laboratory building which is on the other side of Broad St. Our own gas chromatograph is over 13 years old and not capable of doing some of the work we are doing and plan to do. Part-time use of the Clinical Center's apparatus has slowed our own work.

9. Changes in Personnel with Biographical Sketches of new Personnel (append)

See attached sheet.

10. Publications or Papers in Press resulting from the Project or closely related work

See attached sheets.

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11. Budget (for coming year)

A. Salaries (Personnel by names or category)

	% time	Amount
Professional		
Soloff, Louis A.	30%	
Rutenberg, Harold L.	20%	
Lacko, Andras G.	100%	

Technical

Baldwin, F.	100%	
Nickols, P.	100%	
Raja, K.G. Varma	100%	

Sub-Total

Fringe Benefits 12%

B. Consumable Supplies (list by categories)

Chemicals, radiochemicals, glassware,
vials, caps, service, plasma volunteers,
etc.

Heavy Water

7,000

4,000

Sub-Total

11,000

C. Other Expenses (itemize)

Travel for three professionals @ \$500 each
Secretarial assistance

1,500

500

Sub-Total

2,000

D. Permanent Equipment (itemize)

Gas Chromatograph

8,500

75,036

9,980

E. Overhead (15% of A + B + C)

Total

85,016

It is understood that the applicant and institutional officers
in applying for a grant have read and found acceptable
the Council's "Statement of Policy Containing Conditions
and Terms Under Which Project Grants Are Made."

Signature

Director of Project

Signature

Business Officer of the Institution

Telephone

Telephone

Other Sources of Financial Support

List financial support for research from all sources, including own Institution, for this and/or related research projects.

Current

Title of Project

Source

Amount

Duration

The money for the research laboratory building (in which we work) was supplied by a general grant from the United States Public Health Service.

ending

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Publications in 1972

1. On the rate of cholesterol esterification in cord blood serum. Lacko, A.G., Rutenberg, H.L. and Soloff, L.A. *Lipids* 7:426, 1972.
2. In vitro serum cholesterol esterification in coronary artery disease. Rutenberg, H.L., Stern, A.G., Soloff, L.A. and Braverman, S. de. *Amer. Ht. J.* 84:348, 1972.
3. Recovery of labeled cholesterol and cholesterol esters from thin layer chromatograms. Lacko, A.G., Rutenberg, H.L., and Soloff, L.A. *Clinica. Chim. Acta* 39:506, 1972.
4. Serum cholesterol esterification in patients with coronary heart disease: Importance of initial rate of esterification expressed as a function of free cholesterol. Soloff, L.A., Lacko, A.G. and Rutenberg, H.L. *Am. Ht. J.* (In Press).
5. Measurement of the initial rate of serum cholesterol esterification. Lacko, A.G., Rutenberg, H.L. and Soloff, L.A. *Biochem. Med.* (In Press).
6. Abstracts:

Reduced rate of plasma cholesterol esterification in patients with coronary heart disease. Lacko, A.G., Rutenberg, H.L. and Soloff, L.A. *Fed. Proc.* 31:291, 1972.

Esterification of serum cholesterol in hyperthyroidism and hypothyroidism Soloff, L.A., Lacko, A.G., and Rutenberg, H.L. *Circ.* 46: Suppl. II, pg. 224, 1972.

Esterification of serum cholesterol in familial hyperbetalipoproteinemia *Circ.* 46: Suppl. II, pg. 224, 1972.

Submitted for publication:

1. Initial fractional rate of esterification of serum cholesterol in familial hyperbetalipoproteinemia. Soloff, L.A., Lacko, A.G., and Rutenberg, H.L.
2. Serum cholesterol esterification in species susceptible and resistant to atherosclerosis. Lacko, A.G., Rutenberg, H.L. and Soloff, L.A.

Unrelated subjects supported by the Council for Tobacco Research, U.S.A.

1. Asymptomatic rapid ectopic tachycardia induced by and persisting during exertion. Rutenberg, H.L. and Soloff, L.A. *Amer. J. Card.* 29:408, 1972.
2. Clinical significance of the angiographic demonstration of coronary atherosclerosis. L. A. Soloff *Amer. Ht. J.* 83:727, 1972.
3. On the electrocardiogram and clinical improvement of myocardial aneurysmectomy Soloff, L.A. and Rutenberg, H.L. *Amer. Ht. J.* 83:237, 1972.

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4. Cardiac deterioration replacing cardiac pain after surgery to revascularize the heart. L.A. Soloff Amer. Ht. J. 84:446, 1972.
5. An assessment of human cardiac transplantation. Fadali, M. and Soloff, L.A. Amer. Ht. J. (In Press).

Books:

1. Coronary Heart Disease and Coronary Arteriography in Coronary Heart Disease. Grune and Stratton (In Press).
2. Parasystole in Cardiac Arrhythmias. Grune and Stratton (In Press).

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CURRICULUM VITAE

K.G. Varma Raja

REDACTED

Office address: Lipid Research Laboratory, Temple University Health Sciences Center, 3401 North Broad Street, Philadelphia, Penna. 19140

Home address:

REDACTED

Degrees:

- B.Sc. Madras University, Madras, India. Major-Chemistry
minors-Physics and Mathematics.
- M.Sc. University of Baroda, Baroda, India. Major-Bio-
chemistry, minors-General Chemistry and Physiology.
- Ph.D. University of Illinois, Illinois, U.S.A. **REDACTED**

Appointments:

- 1949-50 School teacher, St. Thereas's High School, Trichur.
- 1950-52 Demonstrator, St. Joseph's College, Bangalore.
- 1952-56 Demonstrator, Zamorines College, Calicut, India.
- 1956-58 Research Associate, Fisheries Technological Station
Madras, India.
- 1958-60 Research Assistant, T.B. Chemotherapeutic Center, Madras
India.
- 1967-68 Research Associate, Biology Department, University
of Colorado, Boulder, Colorado.
- 1968-69 Visiting Asst. Professor, Biology Department,
University of Colorado.
- 1969-70 Visiting Asst. Professor and Research Associate,
Johns Hopkins University, Baltimore, Maryland.
- 1970-72 Research Associate Hebrew Geriatric Center and
Hospital, Baltimore, Maryland. Associate, Environ-
mental Medicine, Johns Hopkins Hospital, Baltimore,
Maryland.

Membership:

REDACTED

Fellowship:

Wright Fellow, University of Illinois 1963-66.

Publications:

- K.G. Varma: Effect of para aminosalicylic acid on the loss
of acid fastness in tubercle bacillus by isoniazid. Ind. J.
Med. Res. 49:194, 1961.
- K.G. Varma and S.P. Mistry: Incorporation of glycine into nucleic
acid purines of biotin deficient rats. Fed. Proceedings 25:
784, 1966.
- K.G. Varma and S.P. Mistry: A possible physiological role
of pyruvate carboxylase in the nitrogen sparing action of
carbohydrates. Fed. Proceedings 26:286, 1967.
- Tepper, B.S. and K. G. Varma: Metabolism properties of
purified suspensions of *M. leprae*. J. Gen. Microbiol. 73:143, 1972.

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